ART. III.—*The Practical Application of the Microscope to the Diagnosis of Cancer.* By FRANCIS DONALDSON, M. D., Baltimore, Maryland. With three Plates, representing Cancer and other Histological Elements.

THERE is, perhaps, no disease, not even excepting tubercular phthisis, which has carried off its victims to the grave with more unerring certainty than cancer. For centuries, it has been the dread of the human race. Every child understands that it is some loathsome disease, to be heir to which he would deem the greatest of misfortunes. Its distinctive character has rendered its very name significant of malignancy; the ancient leprosy could scarcely have been regarded with more terror. Its known fatality has made it the study of pathologists of all ages, both as regards its nature and its treatment. Sad is the reflection that, even at this advanced stage of medical science, the inability to cure this disease is still one of those opprobria from which the science cannot rid itself. The physician is still often obliged to look on as a bystander, unable to arrest the malady, literally eating into the very vitals of his patient. We need surely, then, make no apology for adding, if it be merely our mite, to the investigation of this malignant disease.

We have used the microscope in our researches, not merely to satisfy our curiosity, or because the study was interesting in itself, but that we might be able to deduce therefrom its practical application to the diagnosis, and thus, indirectly, to the treatment also. For although, as Dr. Bartlett* remarks, our therapeutics are not deducible from our pathology; yet, it is true, as he proceeds to show, that diagnosis must be in advance of therapeutics.

Some men are disposed to speak of investigations into minute, normal, or pathological anatomy, as if they had no bearing upon the practice of physic; and would draw invidious lines of distinction between the science and the art of medicine, as if a knowledge of the two was incompatible. They forget, or intentionally overlook the fact, that the appropriateness of our treatment must be in proportion to the accuracy of our diagnosis, which, of course, is greater or less, according to the knowledge possessed of pathology. It is true that, after all, the actions of medicines cannot be arrived at from *à priori* reasoning, but by actual experiment, yet pathology must first give the data upon which to found our experimentation.

In answer to the sneer of those who ask whether or not the treatment of disease is more successful, nowadays, based upon scientific principles than it formerly was—whether or not more lives are saved, we do not hesitate to reply, with Dr. Simon, in his recent work on Pathology,† in the affirmative. The negative results alone have, beyond a doubt, saved many a life. Who

* Essay on the Philosophy of Medical Science, by Elisha Bartlett, M. D. 1844.

† Lectures on General Pathology, London, 1851, and Philadelphia, 1852.

can question that the old system of excessive drugging and exhausting blood-lettings, has hurried many a victim to his grave? In this way, alone, the progress recently made in pathology has done incalculable good. Take, for example, Ricord's now well-demonstrated non-identity of syphilis and gonorrhœa. What a bearing it has had upon treatment in preventing the excessive use of mercury! The importance of a knowledge of pathological anatomy and of pathology can be called into question only by those who are ignorant of the true aim of their profession.

It were well to bear in mind that no fact in science is worthless; if we do not now see its practical bearing, it will, sooner or later, be brought forth. M. Chevreul spent a quarter of a century in the study of fatty bodies, one result of which, alone—the use of stearine in the manufacture of candles—was worth all his labour.

A few words to those who object to the employment of the microscope in the investigation of disease. It has been invariably the case that, when any additional mode of exploring disease has been invented, or any discovery made in medical science, many men, who, from their high position, it would have been supposed would cheerfully have supported it, have objected until they were forced to admit it, although, perhaps, they could not avail themselves of it. Harvey, Jenner, and Laennec had to encounter the opposition of those upon whose aid they might have counted. Even to this day, when, if there is a department of medicine which is well established, it is auscultation, there are those found who cavil at it and question its accuracy, although they might as well deny any of the plainest phenomena of natural philosophy. The microscope has, unfortunately, been considered to be a mysterious instrument only to be managed, or even understood, by men of imaginative minds, who could fancy they saw in the field of the instrument any and all conceivable shapes. We are thankful that that erroneous impression is fast fading away, although, in the United States, the practical use of the instrument is not generally understood in its application to medical science. Indeed, the manufacturers have been to blame in no slight degree for this, owing to their unnecessary complication of the machinery. The great number of useless screws and addenda have frightened the profession, and made them believe that, to understand its use, it was necessary to make it one's only study. Then, again, their arbitrary mode of estimating their magnifying powers by the camera lucida, has caused them greatly to exaggerate the power of their lenses. Microscopy, as it is improperly called, some have tried to erect into a new and separate science, when, in fact, it is merely a modification of our ordinary modes of observing—the manner of observing is the only new thing about it. In the examination of those bodies which can be seen well from their size by the natural eye, we do not call in its aid; for those, on the contrary, which are too small to be thus examined, we employ a physical machine, which, by the concentration, &c., of the rays of light proceeding from the object, bring it within the focus of vision. It is nothing

more nor less than an improvement upon our sense of sight. "In this, as in all other improvements in medicine," remarks M. Ch. Robin,* "the first mode of objecting, is to deny the truth of the results; this, overcome by proof, they say that, after all, it is unnecessary, for the existing modes of investigation are sufficient."

But why is there such unwillingness to admit the progress of science? Is it not because the facts revealed, overturn, or more or less modify existing theories, upon which are based all their practical deductions? Was not such the case in the time of the discovery of the circulation of the blood?

If those who think there is no reliance to be placed on appearances in the field of the microscope would take any crystal, such as that of the beautiful octohedra of the oxalate of lime visible already to the naked eye, and magnify it by degrees, they would see that, no matter what the power of the glass used, it possessed the same number of sides, angles, &c.; the only difference being that the minute details, not visible before, would be brought out. They ought to remember that no matter how high the magnifying power of a lens, it cannot render visible things which do not really exist—it cannot create. The only question to be settled is, whether or not a cell or corpuscle of a certain form and size is constantly seen in such and such a normal tissue or morbid growth, and not whether its appearance is the work of the imagination or of some mysterious creating power in the instrument itself. The constancy of the occurrence of the cell, &c., is what gives us a right to classify it as an *element.* We have heard the objection urged that in a few years all we now consider as established will be overturned; new investigations, say they, will do away with existing views; as manufacturers improve in their lenses higher powers will reveal new points. A strange objection this, which would stop all progress in science! Are we to investigate nothing in science because our descendants may improve on our knowledge? But is it correct? Are there no points settled in microscopy? Do higher powers destroy what the lower have shown? Has the highest magnifying lens disproved the constant presence of peculiar corpuscles in the blood? Is there anything clearer than the appearance of the morbid product known as *pus?* Could there be a greater triumph for the truthfulness of the microscope than the now universally admitted fact of spermatozoa in the male semen?—not many years back, and the idea was ridiculed! Have improved glasses done away with M. Donné's researches* in regard to them and to the colostrum corpuscle? Is not the presence of pavement epithelial scales in some parts of the body, and the existence of cylindrical and ciliated ones in others, universally acknowledged? Would not men doubt, if they could, the beautiful phenomena of ciliary motion, such as can be easily exhibited in the oyster, &c., or as can be shown on certain surfaces of the body? We cannot forbear

* Du Microscope et des Injections, Paris, 1849.

† See Cours de Microscopie. Paris, 1844.

mentioning some other points in histology as established by the use of the microscope, such as the muscular fibres of animal and of organic life, the elements of white fibrous tissue, yellow elastic, &c., the fungous vegetable growths in true porrigo favosus, or in herpes tonsurans.* "It is true, the interpretation of these histological elements," observes M. Broca,† "is much discussed." Some think the spermatozoa are animalcules; others, again (the now prevalent, and we believe, the correct view), hold that the motion exhibited is merely ciliary. The exact relation between the Haversian canals of bones and the canaliculi may be disputed, as may the question whether or not white blood-corpuscles are changed from lymph. But the form of these elements and their invariable appropriate presence is not questioned. It is not true, then, that a stronger lens destroys what a feebler has revealed; it must show the same element, only more in detail.

The difference of opinion among microscopic observers, with regard to certain points is no argument against the use of the instrument, any more than the differences among anatomists in regard to coarser anatomy is to be urged against the employment of dissections. The microscope ought no more to be condemned for the errors of the microscopist than the scalpel for those of the anatomist, or chemistry for discrepant analyses. The use of the microscope has already shown the falsity of more than one theory, and abolished more than one hypothesis. "As at the epoch of Morgagni," says M. Broca, "pathological anatomy, though in its infancy, came in contact with the prevailing humoral theory and the empirical doctrines. It was not to be wondered at, that there should have been then, as there ever will be, a violent contest between routine and tradition on the one side, and the progress of science on the other. But here, as in the time of Harvey, when the same contest was carried on with no little ardour, the innovations of science must finally prevail, although at each step it must fight its way."

Our space will not allow of our giving more of the points in histology and in pathology elucidated by the microscope. We can do no more than allude to the settling the disputed nature of the dartos, showing it composed of a peculiar structure of its own; to M. Gosselin's demonstration,‡ that there is properly speaking no medullary membrane, and the confirmation of it by M. Robin;§ to the turning of Bouillaud's views in regard to arteritis, by proving that neither the internal coat, nor, indeed, any coat but the adventitious or outermost of the arteries is vascular, consequently that there can be no such disease as arteritis, so that the coloration taken as inflammatory is merely from imbibition. In the same way, calcareous deposits in the arteries, &c., were erroneously considered osseous in their nature.

* See Des Végétaux qui croissent sur l'homme, &c. Par Ch. Robin. Paris, 1847.

† Quelques Propositions sur les Tumeurs dites Cancéreuses, Thèse. Paris, 1849.

‡ Archives de Médecine. 1847.

§ Mémoires de la Société de Biologie. 1849.

We need scarcely speak of what the microscope has already accomplished in renal and urinary diseases. In that branch of medicine, a physician who is not familiar with the use of the microscope is cut off in his diagnosis from an invaluable aid, as necessary, in fact, for the proper understanding of it, as a knowledge of auscultation is for diseases of the heart and lungs. We need but refer the reader to the manuals of Golding Bird, Griffith, and Frick.

The value of the microscope in forensic medicine should be acknowledged by all, even if its only service had been in detecting spermatozoa and blood-discs, the latter of which, according to Hassall,* can be distinguished in stains six months old.

Thus we see that the microscope has already done good service to the profession, and we may look forward to the not distant day, when its employment, as a means of diagnosis, will be general.†

Certain it is, that we need every possible aid we can get in the difficult work of diagnosis; for how often do we see the most skilful acknowledging themselves baffled. If it was only in very rare cases that the microscope could furnish us with some insight into disease, it would repay the practical physician for the time and labour consumed in pursuing the study. But the fact is, that in numerous cases in every-day practice, its application in medicine renders clear obscure points in disease. It was truly said by Andral, that to it and to animal chemistry must we now look for progress in medical science.

The following deductions in regard to *cancer* have been arrived at from many observations collected during the past three years; eighteen months of which time were passed in Paris, where the material offered for examination was very great. For many of the specimens we are indebted to our friends.

Of course, we have availed ourselves of the results of others; indeed, we have examined all that has been written on the subject within our reach. The existing knowledge of no disease shows so well the gradual progress that has been made in medical science. It may not be uninstructive to trace briefly the doctrines held at different periods as to the nature of this disease. The term *cancer* was applied by the Romans to the morbid condition termed *gangrene* by the Greeks, and *carcinoma* had the signification now generally attached to cancer, being first used to designate certain ulcerations of the mammary gland. The name cancer was supposed to have been given on account of a fanciful resemblance to the body and claws of the crab, remarked in the tumour with its surrounding veins dilated from the obstruction to the return circulation. It may have been, as others conjecture, that the ancients thought there actually existed in the parts affected an animal which devoured the tissues. However, the name, whether originally so intended or not, is

* Microscopic Anatomy of the Human Body. London, 1849.

† It is with peculiar pleasure we welcome Dr. Bennett's new work *Clinical Lectures*, in which the practical use of the microscope is shown in daily practice—a new era in medical literature and hospital instruction.

symbolical of the loathsome and destructive character of the disease. As far back as Hippocrates, who considered *black bile* as its cause, cancer was divided into the ulcerated and non-ulcerated; the former taking the name of cancer proper, and the latter that of scirrhus. After that, the term soft cancer was applied to the morbid product now known as encephaloid. This has been resisted by Abernethy and others, but earnestly contended for by Bayle, who included with them all intractable cutaneous ulcerations.

Ambrose Paré, the father of French surgery, gave his division of cancer, which he thought had its origin in the different kinds of melancholy.

In looking over the catalogue of the various doctrines taught at different periods in regard to this disease, we have been forcibly struck by the indefinite and confused views held on many questions which have been so much elucidated by Corvisart, Laennec, and Bayle in their pathological investigations. Laennec described the physical characters of cancer, and went profoundly into its origin and tendency. His successors, MM. Andral, Cruveilhier, and Velpeau followed in the same train. In England, we owe much to Sir Astley Cooper, for his division of mammary tumours into benign and malignant or cancerous. According to Dr. Walshe,* Dr. Young ought to have the credit of having first classified scirrhus and encephaloid as species of the genus cancer or carcinoma. Dr. Walshe claims for himself, what in justice should belong to Laennec, the having placed *colloid* in juxtaposition with scirrhus and encephaloid as another species.

At this stage of the history of this disease, we cannot refrain from calling attention to the confusion which still reigns in the doctrines taught, which are those held by the majority of modern surgeons, and generally lectured upon in our medical schools. They divide cancer, as did Laennec, into three varieties; but what points do even such authorities as Berard,† Samuel Cooper,‡ or Dr. Warren give us, by which we can distinguish the class of morbid growths, to which they give the indefinite name of *malignant*, without stating in which of the various senses they apply the expression? It is true that close observers noticed that certain exterior characters generally accompanied those tumours which proved fatal. How are we to judge of a tumour in the mammary gland, whether or not it be fibrous, scirrhus, or simple hypertrophy of the proper tissue of the organ itself, either during life or after death? What rules are laid down, even by the most observant and the most skilful, to distinguish what they designate malignant growths from what they call *simple sarcoma?* And again, what definite meaning is attached to this term? If it attacks the bone, it is called osteo-sarcoma; then, again, we have mammary sarcoma, medullary sarcoma, &c., some of which are admitted to be as destructive as cancer, from which many do not separate them.

* The Nature and Treatment of Cancer. London, 1846.

† Dictionnaire de Médecine, en xxx. vols., vol. xv.

‡ Surgical Dictionary.

The lancinating pain, so much relied upon by some, even Abernethy acknowledged could be caused by non-cancerous tumours. We used to be told that, if there was a grating sensation perceived on scraping the cut surface of a tumour, that it was cancerous in its nature; but who has not seen simple fibrous tumours, which have existed for years within the walls of the uterus, in which this sign was perfectly evident?

The term *malignant* must be acknowledged by all to be inappropriate to any one disease, whether applied to designate a sore, which, by ulceration, spreads and destroys life, or to a tumour which has the tendency to recur after extirpation, or as implying a constitutional taint. What more malignant in the sense of destroying life by ulceration, than phthisis; by sloughing, than hospital gangrene; by softening, than ramollissement cerebri? What more destructive than constitutional syphilis? Simple thickening of the pylorus, or any acute ulceration of stomach or intestine could, with perfect propriety, receive the name of malignant. "The only sense in which this favourite term can be applied," justly observes Mr. Bennett,* "exclusively to cancer, is in regard to its returning again;" but, as we shall show, further on, it is true, even in that respect, only in a qualified sense. It would be well if we could, as Dr. Walshe proposed, relinquish altogether the term malignant, as applicable only to cancer; indeed, it would be better still, if the name itself of cancer could be expunged, and some more significant word used. But it is next to impossible to eradicate a word so long in general use, and we must mend the matter by endeavouring to give it a definite and clear meaning.

We do not wish to be understood to say that correct diagnoses cannot be sometimes arrived at by surgeons who judge merely from the coarser physical characters, so to speak, particularly when the disease is located in some exterior organ, and has progressed so far as to ulcerate deeply or to break down the strength of the patient. But we unhesitatingly say that often there is great confusion and doubt even among distinguished surgeons, at the most important period of the disease. We, ourselves, have known of several instances where the great Velpeau, than whom no one has ranked higher as a surgical pathologist, has extirpated as scirrhus of the breast what proved to be nothing more than simple hypertrophy of the proper tissue of the gland. We mean to express our conviction that there can be no just and satisfactory classification of morbid growths not founded upon their intimate microscopic structure; that, if we rely, as heretofore, merely upon their superficial or coarser physical characters, such as volume, consistence, colour, &c., we must often class together things which are, in fact, very dissimilar. This department of surgical pathology without the microscope is just where the diagnosis of diseases of the heart and lungs was, before the discovery of Laennec; or, as obscure and unsatisfactory as the doctrines of essential fevers were before they were distinguished by their anatomical lesions, as when names were given to them

* Cancerous and Cancroid Growths, by J. H. Bennett, Edinburgh, 1849.

according to the grade of febrile reaction, and when, of course, they were often confounded with inflammations.

"We should not be accused," justly observes M. Broca, "of presumption in thus speaking of the errors of distinguished surgeons, our masters. Their ability, their genius, are not denied. We cannot but feel grateful to them, and reverence them. We impute the errors they committed, and the incompleteness of their doctrines, not to them, but to the insufficiency of their means of investigation." The study of auscultation requires no particular talent, yet who can doubt but that any one, who is familiar with it, could diagnose with more accuracy many diseases than could a Sydenham?

The labours of Baillie, Hope, and Laennec, and, in our own times, Cruveilhier, Rokitansky, Barth, Velpeau, and others, have obtained invaluable results from the older methods of research; they had, indeed, apparently made as much advance as could be made in this way. "But," remarks Dr. Lyons,* "the laws of morbid association and the statistics of diseases were yet to be deduced. The microscopist and the chemist have started a new era in pathology, and cleared much which was before obscure."

The use of the microscope had been taken advantage of in many branches of natural science. Botany, Zoology, and Mineralogy have all been greatly elucidated by its employment. Such works as that of Ehrenberg's are seldom met with in any science. It was not to be supposed that the human body would remain unlooked into. As far back as 1722, Leuwenhoeck applied the microscope to find out the intimate structure of our different tissues; but it appears to have been a mere abortive effort, for the science remained nearly dormant for a whole century, when Edwards's, and afterwards Dutrochet's investigations were published. It was not, however, until about the year 1835 that medical science received any impulse in regard to microscopic researches into the minute constitution of cancer. Several prominent men on the continent of Europe commenced their investigations about the same time, but it is principally to the distinguished physiologist, Müller,† that we are indebted for the first microscopic investigation of morbid growths. M. Schwann's theory of cell-formation gave a powerful impetus to these researches. Müller certainly accomplished much in his treatise, for he was the first to attempt to arrange and classify tumours according to their minute composition. He separated enchondromatous tumours, and what he called albuminous sarcoma from cancer. But his work was far from being complete; it was founded, not upon cases observed clinically by himself, but upon specimens handed to him. He did not find a constant element in cancer, because he considered as unquestionably cancer, what the surgeons had extirpated as such. He observed the tumours, but not the patients. Had he compared what he saw anatomically and microscopically with observations at the bedside, there would

* An Apology for the Microscope, by R. D. Lyons, M. D., Dublin, 1851.

† Müller on the Nature, &c., of Cancer, translated by West, London, 1840.

have been more reliance to be placed upon his results. His great merit was in leading the way. It was reserved to M. Lebert, in publishing, in 1845, after unequalled industry and research, the results of his microscopic observations, to define clearly cancer by the microscope.* The first years of his manhood were devoted to zoology and botany, as *Les Annales des Sciences Naturelles* bear good evidence in his many valuable contributions. A good preparation this for his medical studies. He had there learned to observe and to rely upon facts carefully ascertained. He was struck in commencing his medical studies with the absence of that mathematical precision he had always been accustomed to; he found the profession governed more by a science of tradition than by one of observation. He naturally, at once, became a disciple of Louis, whose name will ever be associated with the true starting-point in medical science, he being the first to insist upon the application of the Baconian principles of philosophy to the science of medicine. The adoption of these principles, in all departments of medicine, he saw, as all must, is the only sure way of arriving at anything like an approximation to truth. Based upon such principles, his works, like those of the founder of this era in medicine, must remain forever. His researches on Inflammation; his discovery of the Tubercular Corpuscle; his division of Tumours with the Fibro-Plastic Element; and his classification of Cancerous Growths; his investigations on the Formation of Callus, must ever be valuable. His more recent works (monographs), on Scrofula,† Cancer,‡ and Hypertrophy of the Mammary Gland,§ are justly considered three of the most remarkable and complete treatises ever published. By him it was, that cancer was defined with precision and clearness, and we shall have frequent occasion to quote his authority. It was, in fact, to test, as far as we could, the accuracy of his statements that we have carried on our comparatively limited investigations.

In his recent work,|| he says that years of clinical observation have confirmed his deductions in regard to the cancer element.

Dr. Walshe, in his treatise, has devoted but little space to the consideration of cancer elements.

We may be asked why there is such diversity of opinion existing among such observers as Müller, Walshe, Vogel, Bennett, and Lebert? Why is it that Lebert has been able to draw out with so much more clearness than the others these particular elements? Why so much confusion with others when he has no difficulty? Our answer is to us very plain: the lenses he employs are finer and more powerful. We shall hereafter allude more particularly to the inter-

* Physiologie Pathologique, Paris, 1845.

† Traité Pratique des Maladies Scrofuleuses et Tuberculeuses, par H. Lebert, 1849.

‡ Traité Pratique des Maladies Cancéreuses, &c., par H. Lebert, 1851.

§ De l'Hypertrophie Partielle de la Glande Mammaire, 1850.

|| Traité Pratique des Maladies Cancéreuses, &c. Paris, 1851.

esting work by Mr. Bennett upon this subject. In regard to Vogel's plates,* we doubt if any one can get from them any clear idea of any cell or minute element, with the exception of things which require but a very feeble magnifying power to distinguish them, such as crystals of cholesterine, pus globules, and compound granular corpuscles. He gives as tubercular corpuscles what resemble more than anything else free epithelial nuclei, such as are found in the minute bronchii. His mistakes, and the confusion in which he has involved these matters, are all owing to the feeble lenses employed. According to his own estimate, he saw these corpuscles of tubercle with a power of 220 diameters, when it requires at least 450 diameters to see them at all. We, in examining tubercle, use a lens of Nachet's (No. 7),† of a magnifying power of 833 diameters, according to the most accurate modes of measurement: with this we have no difficulty in describing the corpuscles peculiar to tubercle (see Plate III. Fig. 3), the most constant and unvarying of all. With a triple phosphate crystal, or one of uric acid, which can be well seen with a feeble lens, it is unnecessary to employ higher powers; but with many of the minute elements of the different tissues and products, it is necessary, in order to see them distinctly, to use our highest glasses. With a strong lens there is no danger of confounding pus globules with white blood-corpuscles, or of finding any peculiar globules in mucus. We often hear it said, that for all practical purposes a small microscope with a lens of two or three hundred diameters is all-sufficient. This is a mistake. A microscope, to be applied constantly by a physician, ought to have high as well as low powers, otherwise he can only partially observe. Moreover, these small instruments are without micrometers to measure the diameters of the objects, a very important element of diagnosis; not to mention the absence of a polarizing apparatus, &c. The absurdity of saying, as some do, that there is no confidence to be placed in the accuracy of the higher lenses, is as apparent as the assertion of others who believe nothing but what they can see with their naked, unaided vision. The rays of light passing through lenses placed one above another cannot show what does not exist; if the glasses are achromatic, and have a clear definition, there can be no obscurity. We cannot but think that if Mr. Bennett had used a higher power than 250 diameters, his evidence in favour of the peculiarity of cancer elements would have been much stronger. It is, however, saying a great deal when he admits that the microscope is as useful to the surgeon in the diagnosis of cancer as the stethoscope is to the physician. It would be an exaggeration to say of any rational system, or of any physical sign, that it was a certain, infallible indication of a particular lesion. The observer would, indeed, be narrow-minded and contracted who would rely in forming his diagnosis only upon one of the points attainable, as to the nature of the disease,

* The Pathological Anatomy of the Human Body, by Julius Vogel. Translated by Dr. Day. American edition, 1847.

† With Natchet's *oblique prism*, his short-eye pieces can be used with the high objective glasses, giving a clear definition.

instead of grouping them altogether, giving each its due weight. Does any auscultator rely upon physical signs exclusively, although there are certain of them, the indications of which, even by themselves, are almost pathognomonic? In answer to the question, whether or not we believe there is a peculiar intimate structure, under the microscope, of true cancer, by which it can be distinguished from all other tissue, normal or pathological, we do not hesitate to reply in the affirmative—in the form of clear and well-defined elements.

We do not pretend to say that there may not be shown, in the field of the instrument, a cell about which there could be doubt; nor that, under all circumstances, could a microscopic preparation be pronounced cancer or not. There could not always be such certainty of even anything which is as well marked as striated muscular fibre. But this does not lessen the reliability of our assertion that cancer has its constant element. We believe that, from careful microscopic examination of a piece of fresh tumour, for decomposition or alcohol changes it very quickly, its cancerous or non-cancerous nature can be asserted with confidence. In fine, we hold that the employment of the microscope is more accurate in finding out the structure of cancer than auscultation in defining the exact lesions of the heart and lungs! This we hope to be able to show to the mind of the reader as clearly as we ourselves are convinced of it, by dwelling particularly upon the points of differential diagnosis. At best, auscultatory sounds alone are merely signs of the physical not of the pathological condition. During the past session, we have had several opportunities of exhibiting, to the satisfaction of a class of students, the marked difference between cancer and other elements. The few cells with which Mr. Bennett thinks cancer can be sometimes confounded we will compare side by side, in order that the reader may observe their marked dissimilarity.

We admit that we have examined morbid specimens extirpated as cancer, which did not contain the characteristic appearance, but which were composed generally of either epithelial or fibro-plastic cells. These classes of tumours, Lebert appropriately calls *cancroid*, from their resemblance to true cancer. Mr. Bennett, M. Lebert complains, has extended too far the use of this term, by applying it to nearly all morbid growths, such as cartilaginous, fibrous, fatty cancroid tumours. Has Lebert proved* nothing in regard to the uncertain diagnosis of surgeons, as to the nature of tumours, by showing that Velpeau, Blandin, Malgaigne, and others of the highest reputation, have extirpated as schirrus of the mammary gland what in fact was nothing more than simple hypertrophy of the gland itself?

But, after all, it is objected by some that the microscope can be of no service in the living subject, for it is after death that you discover what caused it, or it is only after an operation you detect the nature of the disease. Even were this true, it would not destroy the propriety of its use as a means of

* L'Hypertrophie Partielle de la Glande Mammaire, Paris, 1850.

diagnosis, for the discovery of *post-mortem* lesions assuredly throw light upon the symptoms manifesting and accompanying them during life. It would be considered absurd to say that the lesion of thickening and ulceration of Peyer's patches is of no assistance in the diagnosis of typhoid fever, because it can actually be seen only after death. The bearing upon the prognosis is not less apparent. But the fact is that, in the case before us, it is possible sometimes to find out the exact nature of the disease before the knife has been used or death supervened. M. Lebert gives several instances where, by the use of his exploring needle, he was enabled during life to withdraw some of the elements of cancerous tumours, and thus diagnose them. Within the last year, we ourselves have been able to diagnose cancer on the living subject, in six instances, by nipping off little projecting points of the ulcerated surfaces. In one case, at the request of Professor N. R. Smith, of a patient at the Baltimore Infirmary, when there was extensive disease, with induration and ulceration of a doubtful character, of the penis; in another, by the kindness of my friend, Dr. Van Bibber, in a patient of his, suffering with a tumour accompanied with deep-seated ulceration of the posterior fauces; in a third, a patient of Dr. Maris's, there was a large encephaloid tumour of the neck; in two cases of disease of the neck of the uterus; and in another ulcerated penis. In all, the microscope revealed unmistakable evidences of cancer.

There is no evading the plain fact that it is almost impossible to give even an approximate definition of cancer as it is generally understood; for it is not a special disease, but a group of affections having in common certain physical characters. It was necessary, in order to give a clear signification to the word, to separate the various morbid growths classed together under the name of cancer. This M. Lebert has been able to do by the aid of the microscope, into three distinct varieties, each having its peculiar characteristic histological element:—

1. *Cancerous tumours*, properly so called, the only ones which should hereafter be so designated, having the cancerous element without analogy in the economy.

2. *Fibro-plastic tumours*, with its peculiar microscopic element; found in certain parts, also, of the healthy structure.

3. *Epithelial tumours*, characterized by the epithelial element, the same as that found as a normal constituent of the epithelium and epidermis.

To render his classification of the various morbid products clearer, M. Lebert draws the important distinction between those elements found normally in the body, to which he gives the name of *homomorphous;* and those not so met with, but as invariably the product of disease or *heteromorphous.* Under this last head he places *cancer, tubercle, pus,* &c.; under the former, *fibres, muscular tissue, white fibrous tissue, fibro-plastic, epithelial elements,* &c. Homomorphous growths can be the product of disease as well as the others.

Before speaking of the microscopic constitution or the *elements* of cancer, let us pass briefly in review the characters of the *tissue of cancer* which is

ordinarily divided into three varieties, *scirrhus*, or hard, stone cancer; *encephaloid*, or soft cancer; and *colloid*, or gum cancer. The first is firm and hard, owing to the amount of fibrous tissue; it is less vascular than the others. The encephaloid resembles the tissue of the brain, and is more or less firm according to whether it is at the commencement stage or further advanced. It is the most vascular kind, and becomes melanotic more readily than either of the others. When it becomes exceedingly vascular, it receives the name of *fungus hæmatodes.* The third, the gelatinous form, has the cancer element mixed with the common uniting tissue; the coloration varies according to the proportion of elements or tissue present. If the former predominate, it has a yellowish tinge; if the latter, the tumour has a transparent aspect. There is a species of tumour which is colloid, but not cancerous, containing fibro-plastic elements combined with cellular tissue. The cases of cancer where there is extravasation of blood, might be designated as another form. To a variety, where the tissue is of a pale, dull yellow, resembling tubercular structure, M. Lebert has given the name of *phymatoïde.* Some writers speak of soft cancer as a degeneration of the hard, but this manifestly is an error; it is, in fact, the more frequently met with even in the incipient deposit. Moreover, all these forms may be seen in the same specimen.

It is improper to attempt to divide cancer into so many species, as they all have the same common pathology. The variety of aspect, consistence, volume, coloration, and vascularity, is caused merely by the amount of fibrous element, of fat, or of gelatinous fluid present; all of which are purely accidental, and in no way essential to constitute the growth. The density, softness, &c., may also vary according to the organ involved; the breast and the pylorus take generally the form of scirrhus; whereas the bladder, the kidneys, &c., are more likely to be affected with encephaloid. Compare the physical characters of cancer with those of the simple tissues, such as the muscular, areolar, dartoric, osseous, &c., or with those of the compound, as the glandular, the synovial, the mucous, &c., and the difference will be very apparent. Its greater or less firmness, its homogeneous fibrous aspect with its lactescent infiltrated juice are very characteristic. The presence of this peculiar fluid is of itself a point of differential diagnosis of great value; the microscope always detecting in it, when found, the presence of cancer cells, &c. No matter what organ is the seat of the disease, this fluid can generally be scraped from the cut surface, or squeezed out by gentle pressure. It is particularly abundant in encephaloid, and frequently oozes out in drops having a white cloudy appearance of the consistence of cream, and very much of its colour, being slightly tinged with yellow. It may sometimes, on superficial inspection, be confounded with light-coloured pus, which has, however, with the yellow, a slightly greenish tinge. If, from the conditions of its formation, there can be any doubt, an appeal to the microscope will at once settle it by giving us the characteristic pus globule. (See Plate II. Figs. 5 and 6.)

The cancer juice forms readily an emulsion with water, and in this differs

from tubercular matter and from that pressed from sebaceous tumours. The colour of this juice, is of course modified by the mixture of other fluids with it; thus, when the vascularity is great, it is often reddish; when from a deposit of dark pigment, we have what is called melanotic cancer, it becomes of a dark brown. When mixed with much fat, it is more consistent; in colloid, it is thicker and sometimes grumous.

We may be asked, what is cancer? If it is meant what is the cause producing the disease so called, we are forced to acknowledge our ignorance; there is a point in regard to this and many other affections beyond which science has not yet fathomed. We know that the disease is peculiar in its nature, in its progress, and in its results; but it is beyond the ken of man to divine what produces the predisposition to its development. To define cancer as a tissue produced by disease is not so difficult. Its fundamental character is the substitution of a new tissue formed of heteromorphous elements for the normal structures formed of homomorphous elements, causing the latter to disappear as it progresses. In the first instance, owing to a peculiar, profound, and inaccessible predisposition, a lymphatic gland, the skin, the bones, or some other part or organ of the body becomes the seat of a local manifestation of disease by the deposit of certain elements foreign to the healthy state. As the malady advances other organs and tissues become involved; and, finally, the whole economy becomes affected, and secondary deposits occur in parts far removed from the primary point of disease.

So thoroughly is the whole system contaminated by the poison, that if the morbid growths be removed, the disease almost inevitably returns; and, finally, produces death. The extirpation was no cure, for the same constitutional cause which originated the mischief, continues to act, and, sooner or later, the reproduction of the evil either in the part first affected or elsewhere will show itself. We do not speak of the certain return of cancer without having the highest authority for our statement. The statistical results given by Dr. Walshe are very conclusive on this point. M. Lebert says, that out of 447 cases observed by him, in and out of hospitals, in which he recognized the microscopic element of cancer, not one case, which could be watched, escaped without a return after extirpation; rarely did even two years elapse before there was another deposit. M. Broca, who, while *interne* under Blandin at *Hôtel Dieu*, had the opportunity of observing a large number of cases, confirms Lebert's statement; in his own expressive words, "le véritable cancer ne pardonne jamais."*

Sometimes, even when the local mischief is not of itself sufficient to cause death, its deleterious effects upon the constitution prove fatal; in fact, occasionally after operations, the body succumbs from the effects of the poison before there is any manifest reproduction of the disease. This unerring fatality cannot fortunately be ascribed to any other of the accidental products

* Quelques Propositions sur les Tumeurs dites Cancéreuses. Paris, 1849.

man is heir to. Cancroid epidermic, or rather epithelial growths, for they are found both externally and internally, can destroy life, and may return after extirpation; but with them the mischief is local, being caused by an excessive production of a normal element; and, consequently, their reappearance is local—at the point where the first existed, but never in parts far removed. Exactly as we sometimes see a return of a common lipomatous tumour *in situ* from all of the original not having been taken out. When death occurs from epithelial tumours, it is from extensive local, not constitutional mischief. They differ anatomically and microscopically from cancer in being in the first instance homomorphous without any deposit of cancerous matter. Epithelial tumours must originate from surfaces covered by epithelium —their growth is slower than that of true cancer. Many of the pretended cases of cutaneous cancer are epithelial, as were doubtless many of Lisfranc's uterine cancers, in which he met with such success. Local injuries sometimes produce them. The mouth, the lips, and the neck of the uterus are their favourite seats.

Cancer is far more malignant than tubercle, which is also a heteromorphous substance, and which proves fatal, not so much from the poisonous effect of the tubercles themselves upon the constitution, as from the abundance of the excretion with the suppuration and ulceration which interferes with the proper action of vital organs. Microscopically, they differ very widely (see Plate III. Fig. 3). Syphilis and glanders (*La Morve*), which, since M. Rayer's researches has elicited so much attention abroad, resemble cancer in one point, that the constitution becomes deteriorated, but they differ in proceeding from without, and not, as in the other, in consequence of a constitutional taint; moreover, there is not with them a particular tissue formed as a result of their contamination.

M. Lebert dwells upon cancer being the substitution of an abnormal element for those which already exist in the body. In proportion as this new tissue is developed, it becomes vascular; nutrition goes on, and the histological healthy structures are compressed, become atrophied, and, finally, disappear. The popular belief of the possible transformation of bone, muscle, &c., into cancer, is totally incorrect. Such is, apparently, the case; but, in fact, the blastema of cancer is thrown out, and the cell and nuclei are formed in the primitive structure; the original elements, being gradually absorbed, give place to them.

We have now arrived at what is, to us, the most interesting point in regard to the disease under consideration, its peculiar element, as seen through the microscope. Taken merely as a tissue with its coarser physical characters, we must all acknowledge it is sometimes difficult even for the most experienced to diagnose it. The question upon which we have already expressed our firm conviction, as to whether or not there are peculiar bodies only found in cancer—when carefully examined, instrument in hand—is one of the greatest importance, both practically and for science. The objections urged,

and the doubts expressed by many who are not familiar with microscopic modes of investigation, are, of course, not worthy of notice. We will, presently, consider Mr. Bennett's views, at which we could not but be surprised, as we had been struck, during a recent sojourn in Paris, with the remarkable unity of opinion there, on this point, among men who now occupy the first rank in scientific matters connected with medicine, such as Rayer, Lebert, Ch. Robin, Claude Bernard, Follin, Broca, and others, members of the "Société de Biologie," and of the "Société Anatomique." We have repeatedly known—as have others who have enjoyed the privilege of attending the meetings of these societies, or of following the *cours* of some of the members—of the same morbid specimen being taken to them to be examined separately, and all to give the same opinion of them.

Some have been rendered incredulous as to the accuracy of the microscope by hearing Velpeau, at his clinique, question it; but, although he has been considered the first surgical pathologist of his day, yet his opinion, in regard to what he has himself never investigated, can scarcely be quoted as high authority. Would that such men would show the same magnanimity as did Louis in regard to the presence of a tubercular corpuscle. He would himself give no opinion, not being familiar with the instrument, but sought that of one whom he knew was, M. Lebert, from whom he gives* a note on the subject.

Some are disappointed on being told that the cancer element is not always of a uniform size, or even of a certain fixed shape; but they certainly do not doubt the existence of epithelial cells because their shape, &c., is different on different surfaces. We will presently show that the great variety of form in the cancer element is a striking peculiarity characteristic of the disease. Notwithstanding their variable form, they all have points of unmistakable resemblance with each other. Out of a hundred individuals of a particular race, there may not be two with precisely the same features, yet about whom there could be no doubt as to their common origin. To use an expressive French phrase, they all have their *cachet particulier*.

In the accompanying plates, we have attempted to arrange (under several divisions), into groups, the different forms of the cancer-cell we have met with. In making the selection from the numerous drawings we have collected in our album, we have thought it better, instead of giving only the types, so to speak, of the several shapes under which we desired to include all the various modifications, to show as many as possible of the numerous varieties. For the rudeness of the designs themselves we ought, perhaps, to apologize, but they are, as far as we could make them, exact representations of what we saw in the field of the instrument. We will first describe the proper elements separately, and then speak of the objections offered by Dr. Bennett, and some others, to their distinct characters as pathognomonic of

* Recherches sur la Phthisie, 2ième édition, Paris, 1843.

cancer, giving drawings of other elements confounded with them. The points of dissimilarity we will call attention to with a view of fixing the differential diagnosis. The mode we have employed has been simply to place between two pieces of glass a drop of the juice, obtained either from gentle pressure, or by scraping the cut surface with a scalpel, diluted with a little water. The cutting off of small slices with Valentin's knife, and examining the whole mass together, will exhibit, almost invariably, more or less fibrous structure, but necessarily the lens employed must be much feebler, and the cell is not seen to the same advantage; moreover, the fibrous element is purely accidental, and is found in a vast number of tumours. The instrument used is a first-class one, manufactured by Nachet. The power we have habitually used in studying cancer element has been one of 555 diameters (Nachet's No. 6). Mr. Bennett used, in his researches, one of 250, which he recommends to others. We state this for the purpose of explaining why it is he has omitted some characters of the element which we believe are of great importance. The element of cancer consists of three parts, *cell*, *nucleus*, and *nucleolus*, all of which are peculiar to it. We will consider—

1. The cancer nucleus, as inclosed in a cell, or as floating free by itself.
2. The polygonal, or more or less spherical and ovoid cell.
3. The caudated cell.
4. The fusiforme cell.
5. The concentric cell.
6. The compound, or mother cell.
7. Agglomerated nuclei connected by amorphous tissue.

In all the varieties of cancerous tissue, nuclei are to be found either enveloped by a cell, or floating free, generally more or less of both; in some specimens, there exists a large number of free nuclei with only an occasional cell. The form and appearance of these nuclei is the most constant and unvarying of all cancer elements. They are (see Plate I. Fig. 1, *a*) ovoid, or more or less round; the latter are found more particularly when the eye or the lymphatic glands are the organs diseased. Sometimes (as in *b*), we find little pieces of the wall of the nuclei apparently nicked out, but evidently it is purely accidental, and the proper shape can easily be recognized. They have, ordinarily, in width, a diameter of from 1-100th of a millimetre, or (a millimetre being equal to .039th of an inch) of .0039th of an inch, to 1-66th of a millimetre, in one instance we met with one as wide as 1-38th of a millimetre; in length they measure from 1-133d to 1-100th of a millimetre. Their contour is dark and well defined, with the interior containing very minute dark granulations; indeed, when the specimen is perfectly fresh, they have a homogeneous aspect, the granulations being so small as to give the appearance of a mere shading (see Plate I. Fig. 1, *c*); if the specimen is kept a day or two, we find the interior filling up with larger granulations (as in *d*). Within these nuclei, when they have not been obscured by granular or fatty degeneration, there is found habitually a small body, or

nucleolus, averaging in diameter about 1-500th of a millimetre. These nucleoli have somewhat of a yellowish tinge, with a brilliant centre and dark borders, refracting light like the fat vesicles. We would call attention, particularly, to the peculiar brilliancy of the centres of these nucleoli, which, we think, is characteristic; it can be almost invariably noticed, if the focus is varied. Their large size, in proportion to the nuclei, should also be noticed, together with the great variableness of their position, sometimes being near the centre, and again in close contact with the walls (see *c*). Ordinarily, in other elements, they are found almost constantly in the centre. Very frequently, two or three nucleoli are found within the same nucleus. M. Robin* mentions the action of acetic acid upon cancer nuclei and their nucleoli, as differing from that on other elements, particularly epithelial; it renders the nucleus gradually paler, together with the cell, destroying neither—but the nucleolus is perfectly untouched by it; whereas in epithelial cells, where generally in those of the skin the nucleoli are wanting, the action of acetic acid destroys the cell, leaving the nucleus unaltered.

It is of primary importance for the proper examination of the cancer nucleoli that the specimen should be fresh. Such being the case, we do not remember ever having found these peculiarities wanting. Mr. Bennett says there is nothing peculiar about the cancer nucleus. But is his opinion to be wondered at, when, often from the low powers used, he could not see at all the nucleolus? The same confusion is produced by Dr. Brinton,† he having used a lens of 200 diameters. A high power as well as a clear definition is necessary.

We have examined some specimens in which free nuclei were in great abundance, and where, after long-continued diligent search, we were unable to discover any cells. More particularly is this the case in cancer of the liver, of the pylorus, and of the lymphatic glands; more rarely in that of the eye. In the breast, many full-formed cells are found with more or less of free nuclei floating in the blastemic fluid. It may be well to remark here that we find also free nuclei of fibro-plastic and epithelial cells, of the finest bronchial ramifications, each with their peculiarities. Mr. Bennett appears to us to have confounded them all together in speaking of what he calls fibro-nucleated tissue.

In regard to the cells themselves of cancer, although we stated their forms as very variable, yet many of them are modifications of the *polygonal,* which may be considered the type. In explanation of the theory of the shape and size of various cell membranes, we would refer the reader to Professor Schwann's views;‡ undoubtedly, as he supposes, the close crowding together, and the processes of endosmose and exosmose, may be the producing cause.

* MS. notes of his Cours de Histologie, 1850.

† Philadelphia Medical Examiner, Dec. 1851.

‡ "Microscopical Researches into the Accordance in the Structure and Growth of Animals and Plants," by Th. Schwann. Sydenham Soc. edit.

Thus we observe that in hard firm tumours, particularly those of the breast and ovaries, the cells found are exceedingly irregular, sometimes nearly triangular. (See Plate I. Fig. 3, f.) The ovoïd or spherical are more frequently met with in soft or medullary cancer (see Plate I. Fig. 3, g), where there is but little pressure, although its juice appears often to be but one mass of cells. It is rare, however, that perfectly round cells are met with, but very generally the angles are well rounded in those which appear to be derived directly from the *polygonal form*, the diameter of which is very variable, ordinarily from $\frac{1}{75}$th to $\frac{1}{25}$th of a millimètre. One peculiarity of this, as of the other forms of cancer-cell, is the presence of the granulations of different sizes in their interior; whereas, in epithelial cells, the interior is generally, when fresh, of course, homogeneous. In cancer, we find the three varieties of granulations given by M. Robin;* *first*, the very fine black dots found in all organic elements, and named by the French, very appropriately, *poussière organique; secondly*, the gray granulations, a form somewhat larger; and, lastly, the fat granulations distinguished by the refraction of the light.—This first variety of cells contains nuclei, having in their interior invariably one or more nucleoli, both of which retain the characteristic points described above. The large size of the nucleus, in proportion to the diameter of its cell, will at once strike the eye of the careful observer.. The variable position, also, of the nucleus within the inclosure, appears to us to be peculiar to cancer; in cells of other structures, the rule is to find the nucleus very nearly in the centre, except with fibro-plastic cells, where the nuclei appear to have a peculiar affinity for the walls. All varieties of cancer cells contain very frequently two or more nuclei; whereas, the epithelial, more particularly those found on the surface of the body (where there is most danger of confusion and doubt), but rarely have more than one. Moreover, the cell of epithelium is much larger than that of cancer, yet the cancer nucleus is twice as large as that of epithelium, as is also the nucleolus, compared with that found in epithelium.

Caudated Cells.—This variety of cancer element appears to be considered *the* cancer-cell by persons unfamiliar with the microscope. The French pathologists speak of it as *la cellule en raquette.* (See Plate I. Fig. 2.) Its general aspect is the same as that of the preceding, the only difference being the prolongations, one, two, or three in number, branching off from the body (so to speak) of the cell; sometimes there are as many as five projections. There is no regularity about them, as the reader may perceive in the plate; indeed, they frequently take the most grotesque shapes.

This form is met with more or less in all cancerous tumours, but invariably in those of the bladder; cancerous degeneration of the parotid often contains them in considerable abundance.

Fusiform Cancer-Cells.—(See Plate II. Fig. 1.) This shape is caused by

* Tableaux d'Anatomie, &c., par Ch. Robin. Paris, 1851.

a swelling in the centre, with the ends pointed, forming often a very acute angle. It is found mixed with the other forms in all parts of the body; but always more numerous in cases where the disease has attacked the bones. M. Robin* says that he has never examined cancer of the bones without finding this variety. It is this form which Mr. Bennett confounds with fusiform fibres of fibro-plastic tissue (see Plate III. Fig. 4), making no distinction between them, but describing them together under the name of *fusiform corpuscles.* Except some similarity of shape, we cannot see how they could be mistaken for each other. We ask the reader to compare the drawing of these two things, and he will at once see that the cancerous is double in width and length; moreover, its nuclei are much larger, and the nucleolus is much smaller in the fibro-plastic, where the absence of the clear bright centre, &c., may be noticed.

The *Concentric Cancer-Cell* (see Plate II. Fig. 2) is formed of an ovoid or spherical body, surrounded by concentric rings, so as to give the peculiar appearance of circles around a centre, increasing in size as they get further out. The centre resembles in every respect the ordinary cancer nucleus, and sometimes other nuclei appear between the circles, and occasionally a nucleus is seen pressing against the outside of the cell wall. It is not known how this variety of cancer constituent is formed, and we forbear giving any of the conjectures in regard to them. Sometimes a mass of epithelial cells are pressed together, and present somewhat this appearance. This cell is met with but rarely, and but few in a specimen; it is more likely to be seen, says M. Robin, in the uterus, breast, and ovaries, than elsewhere; it never forms the basis of the tumour, but is merely accessory. According to Robin, it exists more frequently in the form of cancer tissue, which, in consistence, is between schirrous and encephaloid.

Having ourselves but one drawing of a distinctly marked specimen of this cell, we borrow for our plate one from M. Lebert.†

The *Compound or Mother-Cell of Cancer* (see Plate II. Fig. 4) is of very variable shape, as the drawings show. They have received this name from the views entertained by some authors, more particularly Küss and Bruch, of their splitting up into smaller segments and multiplying by division. They contain often three, four, or more cancer nuclei. We ourselves have never seen more than seven within one cell, although Lebert gives a drawing of one containing as many as nine. Some consider that secondary cells are formed within the parent one, and are let out by the rupture of the outer wall. It is, however, mere conjecture.—The last form in which these elements are exhibited is where a number of nuclei appear to be glued together, as it were, by the amorphous blastema in which they are generated, without there being any recognizable cell wall around them. M. Robin‡ calls them *plaques à*

* MS. Notes of his Cours d'Histologie, 1850.

† Physiologie Pathologique. Atlas, Plate XVIII.

‡ Tableaux d'Anatomie, 1851.

noyaux multiples. The size of the envelop about them prevents them from being confounded with anything else. These *agglomerated nuclei* (see Plate II. Fig. 3) are nearly as rarely met with as the concentric cell.

All these varieties of cancer element can be seen in the same specimen, although, as we mentioned in speaking of each, they have separately organs of selection. Cancer cells, of course, like homomorphous elements of the organized animal or plant, have their periods of growth, and development, and decay; their progress to maturity may be sometimes arrested, and account to us in some measure for the great variety of appearance, structure, and size. For some interesting remarks, in regard to the retrograde metamorphosis of all tissues, both normal and pathological, we would refer the reader to an article by Dr. Burnett.*

Out of the body, cancer elements change very rapidly, more so than any one element we have met with. Often, in the course of the first day, they become degenerated by the appearance of fatty granulations, which often hide their distinctive characters. Unfortunately, they cannot be preserved in any fluid. Alcohol coagulates the albuminous cell wall. Mixed up with what we have designated cancer elements are often found crystals of cholesterine and of triple phosphates of ammonia and magnesia, filaments, fat globules, crystals of margarine, pus (see Plate II. Figs. 5 and 6), &c. Wherever there is inflammation, especially of a chronic character, we are apt to find fibro-plastic elements; consequently, we must not hastily conclude, because we find them in a tumour, that there is nothing else there. The importance, therefore, of examining thoroughly, as far as possible, each portion of the specimen, cannot be urged too much. If but one cancer-cell be found, it is conclusive. That which has been designated *melanotic cancer*, is merely a mixture, with true cancer elements, of free pigmentary granulations, or of the peculiar cells of pigment.

We have already given our belief as to whether or not these elements are so characteristic that none others, either normal or pathological, can be confounded with them. Some authors of high standing have asserted that such is not the case. Vogel admits that the cancer element is sometimes characteristic; but, judging from his drawings, we should say he used the same power he did in examining the triple phosphates, 90 diameters. Dr. Walshe, in his otherwise complete monograph, devotes but little attention to the histological arrangement under the microscope. Mr. Bennett is the most serious opponent to the diagnosis of cancer by the use of the microscope. With all due regard for one so eminent in the scientific world, we are forced to state the impression a careful perusal of his work has left upon our minds—that he repeatedly contradicts himself. In some places, he gives the characteristic appearance of the cancer element, which he so names, and then again he speaks of epidermic cells becoming cancerous. In one place, he speaks as though the appearance

* American Journal of the Medical Sciences, July, 1851.

he admits generally found in cancer was merely a state of development of normal elements. He says, in part of his treatise, that such and such cells are characteristic of cancer, and then, afterwards, of epithelial cells steeped in water, resembling, in every particular, cancer-cells, and of young epithelial cells also being indistinguishable from them. He concludes by drawing the diagnosis of cancroid growths (the signification of which he has extended so as to destroy the definition given to it by Lebert, who invented it) as not containing the cancer element, and yet he denies there is any cell, &c., only found in cancerous growths! We give, however, that others may compare them, the histological elements with which Mr. Bennett thinks cancer can be confounded.

In regard to epithelial elements, we give (Plate III. Fig. 1), young epithelial cells from Lebert's plate, and we think it unnecessary even to call the attention of the reader to the general aspect of the cell, the proportion the nucleus bears to the cell, the absence of any nucleolus, &c.; the other varieties, ordinary tessellated scales (Fig. 2), cylindrical and ciliated (Fig. 4), could scarcely be mistaken for any other element. We draw (Fig. 9) pavement epithelial, seen with the same power we used with the cancer elements.

Fibro-plastic elements possess a peculiar interest in being the only ones where there is any ground for seeing a resemblance to cancer elements. They were first defined by M. Lebert, who thought them always the product of disease. Further researches have convinced him that such is not the case. In the healthy subject, they are found in the bladder, ovaries, liver, mammary gland, uterus, &c. According to Robin,* the internal membrane of the Graafian vesicle is the only membrane, in the state of health, which is formed altogether of it. The discovery of them in the uterus is due to M. Robin, who has confirmed M. Coste's interesting researches in regard to the hypertrophy of the uterine mucous membrane during the evolution of the Graafian vesicles, and in regard to the same membrane forming the coverings of the fœtus, known as the *decidua vera* and *reflexa*, by finding that the fibro-plastic cells, as one of its habitual elements, actually become larger as the first stages of pregnancy advance.† It is, moreover, fibro-plastic tumours which are the true sarcomatous ones, and which are so frequently confounded with cancer. Their slow growth, the absence of the cancer juice, their return after the operation *in situ*, but not elsewhere, showing there is no constitutional taint; their being frequently encysted, which cancer never is; their carnified consistence, and their having the cellular tissue as their point of departure, and generally not organs, are important diagnostic signs.

We give the true fusiforme corpuscle (Plate III. Fig. 4) of this tissue, the length of which is often as much as from $\frac{1}{18}$th to $\frac{1}{31}$st of a millimetre. The narrowness of their width, the smallness of their nuclei, the nucleolus, and, indeed,

* MS. Notes of his Cours d'Histologie, 1850.

† See Traité Pratique des Accouchments par Cazeaux, 3ième edit. Paris, 1850.

the whole aspect, would prevent, we should think, any one who is familiar with microscopic investigations, from confounding them with anything else. The fibro-plastic cells and their free nuclei (Fig. 5) could be mistaken for cancer by a superficial observer. They are ovoid, and sometimes polygonal, varying in diameter from $\frac{1}{200}$th to $\frac{1}{66}$th of a millimetre. The appearance, however, of the nucleus itself with the nucleolus, differs very widely from cancer, the granulations in their interior are very much finer, and of more uniform size than those found in cancer. The free nuclei of fibro-plastic tissue are so much smaller as to be easily known when met with.

But the strangest comparison we find in Mr. Bennett's book is between cancer and cartilage elements. Since Müller's articles on enchondromatous tumours, the attention of pathologists has been much turned to their investigation. Had we the time and the space we would describe particularly the elements of cartilage, which compose this class of morbid growths, and which are as clearly marked as striated muscular fibre or any other histological element. Suffice it now to remark that within a homogeneous structure, composed principally of gelatine, and called hyaline, are found excavations or cavities measuring often more than one-twentieth of a millimetre, more or less of an irregular ovoid shape, with cells (not corpuscles as was formerly supposed), generally of one-fiftieth millimetre in diameter, which contain a nucleus often filled with fatty granulations, so as to destroy the nucleolus. The hyaline structure invariably accompanies them, and bounds them on all sides; this has been considered so characteristic of cartilage as to preclude all danger, independent of the form of the cell, of its being mistaken for anything else.

Mr. Bennett tells us, that when enchondromatous tumours become softened, and the cells escape from the cavities they resemble very closely cancer. It has never been our good fortune to meet with any such cases, but we confess we cannot understand how, even if the cells were free, they could be taken for those of cancer. Compare them (Plate III. Figs. 7 and 8) with any or all of the varieties of cancer element (Plates I. and II.), and remark the difference of shape, &c.

In Plate II. Fig. 5, we give a drawing of *pus*, before the addition of any reactive, and, in Fig. 6, we give the same corpuscles, acted upon by acetic acid. It will be noticed that with a high power, frequently a dim outline of the nuclei can be seen when the corpuscles are unmixed with any reagent. We are glad to have the support of Bennett and Robin in stating that there is no mucus-corpuscle. What has been so called was either pus, so easily produced on mucous membranes, or epithelial nuclei.

Thinking it would be not uninteresting to the reader to compare the element of tubercle with that of cancer, we give (Plate III. Fig. 3) several corpuscles found in a specimen of softened tubercular lung handed to us while copying off these remarks; from the first preparations examined we could have given almost any number, but the few we have drawn are perfect type specimens.

A few words in conclusion, in regard to the development of cancer. We forbear saying anything of the absurd theories of its being produced by infusoria, &c. Of where and how it originates we must acknowledge our ignorance. That the materies morbi, whatever it may be, is propagated by the blood it is rational to suppose; but certain it is, the element of the disease is never there found, no matter how contaminated the whole system may have become. We think that M. Lebert has proved, in his researches on inflammation,* that pus, inflammatory corpuscles, pyoid globules, &c., are never formed within the bloodvessels, but entirely external to them in the effused liquid; indeed, even the three blood globules are too small to exude through the coats of the capillaries; the red colouring matter, the hematine, may discolour the effused serum; but if any blood-globules, even to the minute globuline, are discoverable, there must necessarily have been a rupture. This fact is one of vast importance in questions of pathology in regard to the absorption of pus, &c. The cause of the development of cancer is still inexplicable, but we know that in the nutritive material thrown out there is cancer blastema mixed up with it, and that the elements of cancer are formed together with those of the organ or tissue where it is developed. After this, the cancer tissue is nourished as are the healthy structures.

Dr. Walshe carries out Schwann's cellular theory in regard to cancer to its greatest extent, and thinks cancer is propagated by the generation of cells from cells, but his conclusion was a theoretical one. We need not apologize for quoting so frequently M. Lebert, who states that after having carefully for years examined, both before and since the publication of Schwann's work on embryonic cells, the cells, &c., of the adult in the healthy tissues, and in morbid products, he is convinced that, in morbid tissues especially, each and every cell, fibre, &c., is formed separate and apart from the cancer or other matrix, or blastema. Thus a new deposit of blastema is necessary to give rise to new cells. At first a small nucleus is formed, which becomes larger and larger, then gradually a nucleolus is formed in the centre, and the whole is enveloped in a cellular wall, which swells out by endosmose, until it reaches the usual type, size, and form. It can become deteriorated by diffusion, by rupture of its walls, from internal granulations, either molicular or fatty, by atrophy, &c. In this way, the cells are formed from the matrix, and not from direct cellular generation, and disappear, and are not, and cannot, indeed, be taken as such into the circulation.

There is, perhaps, no doctrine or statement in medical science, which has had so universal an acceptance as that of M. Schwann's, in regard to cell-formation; with him, all the tissues must necessarily, both vegetable and animal, pass through the transition state of cells. All, it appears to us, will be surprised, if they read Schwann's work itself, to see upon how slender a foundation he erected such a superstructure, as the universal application to the

* See Physiologie Pathologique, t. i.

tissues of all kinds and sorts, of the cellular theory of formation. Henle believes that nuclei are the primitive elements formed.

But we have what to us is the highest authority against the entire adoption of Schwann's views as applicable to all organisms in the researches of MM. Lebert and Robin. In a recent publication by M. Robin,* he defines with his usual clearness the doctrines professed by him on this subject. He says that strictly speaking there is great misapplication of the term *cell*, which is a small body with a wall, a cavity, and a contents. This exists in most of the vertebrata only during embryonic life, when the being is composed entirely of cells. When it becomes a fœtus, *fibres*, *tubes*, &c., form; cells, properly speaking, disappear, and together with the fibres, &c., a flat body is formed, to which the term of cell is generally applied, which is a mass of the same density in the centre as at the periphery, without a true wall or a contents, with a nucleus in the centre. There are, however, some few exceptions to this; in certain glands the elements retain their walls, cavities, and contents; this is more particularly the case in invertebrated animals. M. Robin, then, acknowledges that the cellular theory is true, so far as it relates to the fact that all animals and vegetables derive in the first instance their structures from cells; that is, that they are born from cells which are formed by the segmentation of the yolk of the egg. These cells, however, are transitory, properly speaking, *embryonic*, because they there end, and are destined to be replaced by permanent elements; in the human subject, the embryonic life only continues until the eleventh day after conception. So far Schwann's view holds true; the animal is during embryonic existence as the vegetable; but the originator of this beautiful theory would carry his doctrine much further, even into fœtal and adult life. M. Robin professes that, during and after fœtal life, there is one of two processes in the formation of the elements of the tissues, organs, &c.: either there is a direct metamorphosis of the embryonic cell by a change in its form, volume, consistence, &c., into anatomical elements, such as cells of the epidermis, &c., or else there is a substitution of entirely new elements for it, which are formed altogether independently of it in a new cytoblastema.

This process of metamorphosis is universally true in the vegetable world, but only in the animal as regards what he calls *les produits*;† that is, those parts, which although derived from the tissues themselves and capable of being reabsorbed, are yet not part of, nor essential to them; that is, those which have merely a vegetable function, including therein more than we express by secretions and excretions. Some of these *produits* are destined to be at once ejected without serving any purpose in the economy, such as the urine, the feces, the sweat, &c. Others of them, on the contrary, as the

* Supplément au Dictionnaire des Dictionnaire de Médecine, article Ostéogénie. Paris, 1851.

† See Preface to "Du Microscope et des Injections, &c." By Ch. Robin. Paris, 1849.

saliva, gastric juice, bile, pancreatic secretion, the sperm, the epithelium, &c., are needed, and are used by the system for the protection of the body, preservation of the species, promotion of nutrition, &c. In these, there is a transformation of the true commencing cell into new elements.

Les constituants, the tissues themselves; that is, those parts which have animal as well as vegetable functions, are formed by the second process, the *substitution* of new and permanent elements for the transitory or embryonic cells, which disappear entirely. In one word, a new matrix is effused in which there is a spontaneous generation of new elements in each tissue, the old being dissolved or reabsorbed, and playing no part in the new formation. This mode of formation by substitution exists only in the animal, and with it merely in regard to the constituents of their tissues; these elements are of a permanent kind, and are generally in the form of tubes, fibres, homogeneous uniting tissue, &c., and but rarely of cells; the reverse of this is the case with *les produits*.

M. Lebert, in his researches on inflammation, watched very closely under the microscope in wounds of animals the formation of fibres, cellular tissue, &c., and he tells us that they acquired immediately their permanent shape without going through any cell stage. True muscular fibre cannot be reproduced after fœtal life.

These three orders of facts, it will be remarked, are very closely linked together.

The *cellular theory* is true of embryonic life for both vegetables and animals.

The *theory of transformation* is applicable to the formation, during fœtal and adult life, of all the elements of vegetables, and merely to those parts of the animal which have only vegetable functions to perform.

The *theory of substitution* applies in no particular to the vegetable kingdom, but solely to the formation of the anatomical elements of the animal tissues.

We hope the reader will pardon our prolonging this paper by this digression, but we felt grateful to M. Robin for giving the right direction to, and thus modifying, after devoting years to the investigation of the phenomena of the formation and growth of our tissues, the extravagant theory of Schwann, which some have thought almost explained all the phenomena of life. We say we felt so much indebted to him for all these and many other valuable truths communicated by his works and orally, that we could not forbear giving these beautiful results to the lovers of science in this country.*

* Since writing the above, our attention has been drawn to Dr. Pope's translation, in the September number of the *St. Louis Medical and Surgical Journal*, of M. Broca's thesis.

Baltimore, *October*, 1852.

Fig. 1.

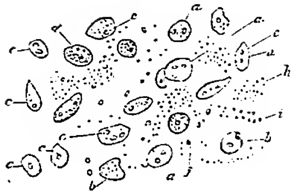


Fig. 2.

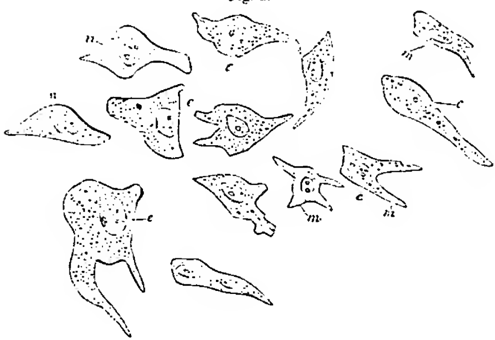


Fig. 3.

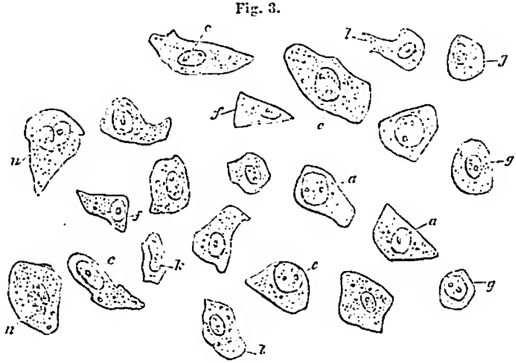


Fig. 1.

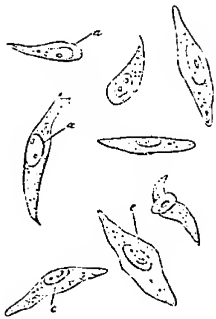


Fig. 2.

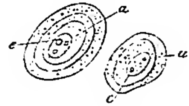


Fig. 3.

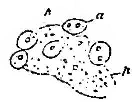


Fig. 4.

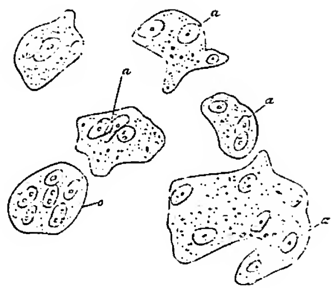


Fig. 5.

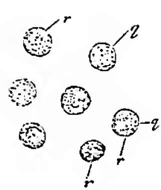
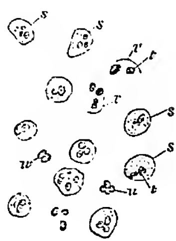


Fig. 5.



EXPLANATION OF PLATES.

PLATE I.

[ALL THE CANCER ELEMENTS IN THESE PLATES ARE MAGNIFIED 555 DIAMETERS.]

FIG. 1. *Free cancer nuclei; a*, type form; *b*, the same with a piece nicked out of the side accidentally; *c*, shows a free nucleus, in which the molecular granules are very minute, often met with in perfectly fresh specimens; *d*, a nucleus, in which larger granules have commenced to form; *e*, the characteristic nucleolus with its dark contour and bright centre; *h*, fine molecular granules; *i*, the second variety of granules, or gray granulations; *j*, fat granules.

FIG. 2. *Caudated cancer-cells; m*, the most usual forms; *n*, cells containing double nuclei; cancer of the bladder invariably contains this variety.

FIG. 3. Forms of *cancer-cells* derived from the *polygonal* or type variety; *g*, spherical cells; *a*, dark contour of inclosed nucleus; *c*, the nucleolus; *k*, a nucleus with its contour pressed out of shape; *l*, a form of cell frequently seen, where there is a deficiency of part of the wall; *f*, from pressure rendered triangular.

PLATE II.

FIG. 1. *Fusiform cancer-cells*, found in great abundance in cancerous disease of bones; *a*, the nucleus, which, in this variety of cell, is almost constantly ovoid. The transverse diameter of the cell and the size of the nucleus in proportion to the cell, together with the characteristic nucleolus, distinguish this variety from the fusiform fibro-plastic element.

FIG. 2. Two *concentric cancer-cells; a*, the cancer nucleus, the size of which is always in proportion to the innermost circle; *c*, the brilliant nucleolus.

FIG. 3. *Agglomerated nuclei*; *a*, nucleus; *p*, amorphous uniting tissue.

FIG. 4. *Compound cancer-cells*, containing three or more nuclei; *a*, nucleus; when there are more than one nucleus within a cell they are smaller than the single nuclei; *o*, from Lebert.

FIG. 5. *Pus corpuscles*, magnified 833 diameters; *q*, type form before the addition of any reactive; *r*, outline of nucleus seen surrounded by thick granulations.

FIG. 6. The same after the application of acetic acid; *s*, the irregular contour of the corpuscle freed from the granulations, leaving the nuclei clear; *t*, characteristic nucleus without any nucleolus; *u*, free nuclei, the walls having been destroyed. Diameter of pus-corpuscle varies from 1-100th to 1-80th millimetre, that of the nucleus 1-333d; r, remnant of contour.

PLATE III.

FIG. 1. *Young epithelial cells* (from Lebert's plate); *w*, cell-wall filled with few and small granules; *x*, the nucleus, very small in proportion to cell, and containing no nucleolus.

FIG. 2. *Tessellated epithelium; y*, nucleus without nucleolus, diminutive in proportion to cell; *z*, the cell with homogeneous minute granulations filling up the centre. Diameter of the cell when taken from the skin 1-10th millimetre.

FIG. 3. *Corpuscles of tubercle* (833 diameters); 1, corpuscles found in softened tubercular matter; a small irregularly formed globular body with neither nucleus nor nucleolus, measuring 1-142d millimetre in diameter; 2, interior granulations; 3, free loose granulations.

FIG. 4. *Fusiform corpuscles of fibro-plastic tissue;* 4, the narrow and long fusiform cell, containing a nucleus (5) with a small dot in its centre for a nucleolus; average length of cell 1-12th millimetre. (Magnified 555 diameters.)

FIG. 5. *Spherical fibro-plastic cells*, found in the uterus and in other organs in the healthy subject; also as the result of chronic inflammations; and forming, with the preceding variety, the basis of true sarcomatous tumours: 6, well marked cell: 7 and 8, nuclei inclosed in cells or floating free; transverse diameter 1-200th millimetre.

FIG. 6. *Cylindrical and ciliated epithelial elements*, found in the nasal fossæ, trachea, Eustachian tubes, in the intestinal canal below the cardiac orifice; 9, hair-like extremities, which, during life, are constantly in motion; 10, nucleus clear in the centre.

FIG. 7. *Cartilage elements taken from the condyles of the femur;* 13, hyaline tissue: 14, excavated cavity; 15, cartilage cell; 16, nucleus; 17, nucleolus very frequently drowned by the fatty granulations.

FIG. 8. *Costal cartilage;* 18, hyaline substance; 19, cartilage cavity; 20, cell; 21, nucleus.

FIG. 9. *Buccal epithelial scales*, magnified 555 diameters, to show more clearly their dissimilarity to cancer elements; 11, irregularly polygonal contour; 12, the characteristic nucleus without any appearance of a nucleolus, which is rarely met with in epidermic cells, or in those coming from the buccal surface.

Fig. 1.

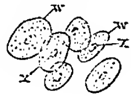


Fig. 2.

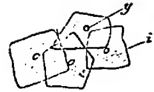


Fig. 3.

Fig. 4.

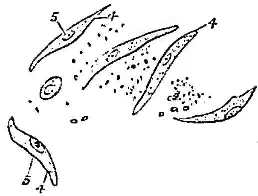


Fig. 5.

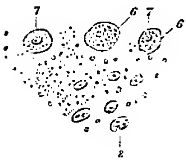


Fig. 6.

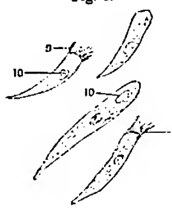


Fig. 7.

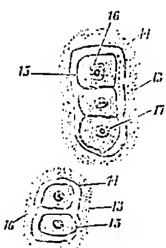


Fig. 8.

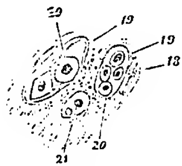


Fig. 9.